

## **REMARKS**

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-49 and 52-56, as well as new claims 57 to 63, the only claims pending and currently under examination in this application.

### **FORMAL MATTERS:**

Claims 1, 26-28, 30-33, 35-36 and 43-49 are currently amended. Support for the amendments is found in the specification at least at paragraphs [0046], [0049] and [0103]. Support for the terms “directly detecting” is found at least at paragraph [0137] and Fig. 5A where the signal probe was directly detected in the presence and the absence of the quencher.

New Claims 57-63 have been added. Support for the new claims is found in the specification at least at paragraphs [0104] and [108].

These amendments add no new matter to the application and their entry by the Examiner is respectfully requested.

### **INTERVIEW SUMMARY:**

The Examiner is thanked for the telephonic interview held on May 14, 2008. During the interview, the above amendments were discussed in the context of the current rejections. Examiner Salmon indicated that the proposed claim amendments would overcome the §112, second paragraph rejection. With regard to the §102(b) rejection, Examiner Salmon indicated the proposed amendment of “directly detecting” in the claims would overcome this rejection. The proposed combination of the Wittwer and Tyagi citations was discussed, but no agreement was reached. It is believed that above summary provides a true account of the substance of the personal interview.

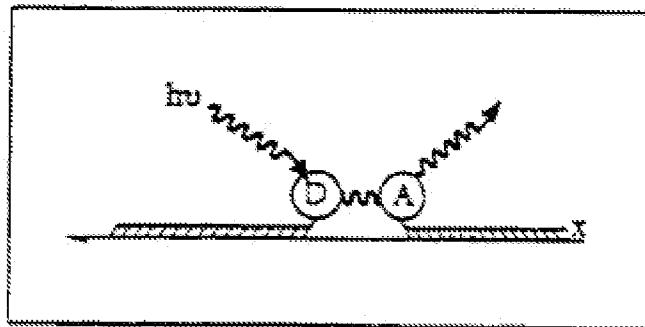
### **REJECTIONS UNDER §112, SECOND PARAGRAPH**

The Examiner has rejected Claims 1-49 and 52-56 under 35 U.S.C. §112, second paragraph. The claims as currently amended no longer include the objected to terminology. Accordingly, this rejection may be withdrawn.

### **REJECTIONS UNDER §102(b)**

The Examiner has rejected Claims 1-4, 6, 9-10, 26-28, 31-33, 36-44 and 46-49 under 35 U.S.C. §102(b) as allegedly being anticipated by Wittwer et al., (U.S. 6,140,054; henceforth “Wittwer”) The Applicants respectfully traverse the rejection.

The claims as currently amended specify that the signal probes are directly detected. In contrast, Wittwer teaches a method of fluorescence energy transfer (FRET) wherein the fluorescence energy of a donor probe is transferred to an acceptor probe which then emits a detectable signal. In Wittwer’s method, the signal that is detected is from the acceptor, as illustrated in reproduced FIG. 3B below.



**Fig. 3B**

Because Wittwer uses FRET, there is no direct detection of the signal probes. Therefore, Wittwer does not disclose every element of Claims 1-4, 6, 9-10, 26-28, 31-33, 36-44 and 46-49 and the rejection of these claims under 35 U.S.C. §102(b) over Wittwer may be withdrawn.

### **REJECTIONS UNDER §103(a)**

The Examiner has rejected Claims 11-15 under 35 U.S.C. §103(a) as allegedly being obvious over Wittwer in view of Tsourkas et al., (N.A.R. (2002) 30:5168 (henceforth “Tsourkas”). The applicants respectfully traverse this rejection.

In order to meet its burden in establishing a rejection under 35 U.S.C. §103, the Office must first demonstrate that a prior art reference, or references when combined, teach or suggest all claim elements. See, e.g., KSR Int’l Co. v. Teleflex Inc., 127 S.Ct. 1727, 1740 (2007); Pharmastem Therapeutics v. Viacell et al., 491 F.3d 1342, 1360 (Fed. Cir. 2007); MPEP § 2143(A)(1).

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the self-indicating probe element. For this element, the Examiner looks to Tsourkas.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Tsourkas was cited solely for the element of self-indicating probes, Tsourkas fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Tsourkas fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 11-15 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tsourkas and this rejection may be withdrawn.

The Examiner has rejected Claims 11-15 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Sokol et al., PNAS (1998) 95:11538 (henceforth “Sokol”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the self-indicating probe element. For this element, the Examiner looks to Sokol.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Sokol was cited solely for the element of self-indicating probes, Sokol fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Sokol fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 11-15 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Sokol and this rejection may be withdrawn.

The Examiner has rejected Claims 11, 16-20 and 38 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Kubista et al., U.S. 6,329,144 (henceforth “Kubista”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the self-indicating probe element. For this element, the Examiner looks to Kubista.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Kubista was cited solely for the element of self-indicating probes, Kubista fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Kubista fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 11, 16-20 and 38 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Kubista and this rejection may be withdrawn.

The Examiner has rejected Claims 11 and 21-23 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi et al., U.S. 6,277,607 (henceforth “Tyagi”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the intercalating dye element. For this element, the Examiner looks to Tyagi.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Tyagi was cited in this rejection solely for the element of the intercalating dye, Tyagi fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Tyagi fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 11 and 21-23 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi and this rejection may be withdrawn.

The Examiner has rejected Claims 24-25 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Singer et al., U.S. 6,323,337 (henceforth “Singer”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the fluorescent minor groove binding dye element. For this element, the Examiner looks to Singer.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Singer was cited in this rejection solely for the element of the minor groove binder, Singer fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Singer fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 24-25 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Singer and this rejection may be withdrawn.

The Examiner has rejected Claim 45 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Schalasta et al., Infection (2000) 28:85 (henceforth “Schalasta”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the virus genotyping element. For this element, the Examiner looks to Schalasta.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Schalasta was cited in this rejection solely for the element of the virus genotyping, Schalasta fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Schalasta fails to teach or suggest all of the elements of the claimed invention. Therefore, Claim 45 is not obvious under 35 U.S.C. §103(a) over Wittwer in view of Schalasta and this rejection may be withdrawn.

The Examiner has rejected Claims 5 and 7-8 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Caplin et al., Biochemical (1999) 1:5 (henceforth “Caplin”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the element of melting temperature differences between probes. For this element, the Examiner looks to Caplin.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Caplin was cited in this rejection solely for the element of the melting temperature differences between probes, Caplin fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Caplin fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 5 and 7-8 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Caplin and this rejection may be withdrawn.

The Examiner has rejected Claims 29 and 34 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Marras et al., N.A.R. (2002) 30:122 (henceforth “Marras”).

The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the element of the temperature rate change. For this element, the Examiner looks to Marras.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Marras was cited in this rejection solely for the element of the temperature rate change, Marras fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Marras fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 29 and 34 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Marras and this rejection may be withdrawn.

The Examiner has rejected Claims 29 and 34 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Elenitoba-Johnson, U.S. 6,346,386 (henceforth “Elenitoba-Johnson”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the element of the temperature rate change. For this element, the Examiner looks to Elenitoba-Johnson.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Elenitoba-Johnson was cited in this rejection solely for the element of the temperature rate change, Elenitoba-Johnson fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Elenitoba-Johnson fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 29 and 34 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Elenitoba-Johnson and this rejection may be withdrawn.

The Examiner has rejected Claims 30 and 35 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Wittwer et al., U.S. 6,245,514 (henceforth “Wittwer B”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the element of the rate of monitoring of the detectable signal. For this element, the Examiner looks to Wittwer B.

However, as demonstrated above, Wittwer does not teach a method in which the signal from the signal probe is directly detected. Nor does Wittwer suggest this element because Wittwer relies on the two probe FRET protocol in order to obtain a signal only when the target sequence is present. As Wittwer B was cited in this rejection solely for the element of the rate of monitoring of the detectable signal, Wittwer B fails to make up for this deficiency in Wittwer.

Accordingly, the combined teaching of Wittwer in view of Wittwer B fails to teach or suggest all of the elements of the claimed invention. Therefore, Claims 30 and 35 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Wittwer B and this rejection may be withdrawn.

The Examiner has rejected Claims 1-4, 6, 9-12, 14-15, 26-28, 31-33, 36-44 and 46-56 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko et al., Biotechniques (2001) 31:1106 (henceforth “Didenko”).

The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that Wittwer teaches all of the elements of the claims but for the element of directly detecting the signal from the signal probe. For this element, the Examiner looks to Tyagi and asserts that it would be obvious in view of Tyagi to modify Wittwer to look at the signal from the signal probe as opposed to the signal from the acceptor.

As reviewed above, Wittwer discloses a two probe FRET system which is based on two separate probes being brought into close proximity by binding to a target sequence of interest. When the two probes are brought into close proximity, one can detect an emitted signal from the acceptor fluorophore as a positive indication that the target sequence is present. The FRET approach of Wittwer is illustrated in FIG. 3B.

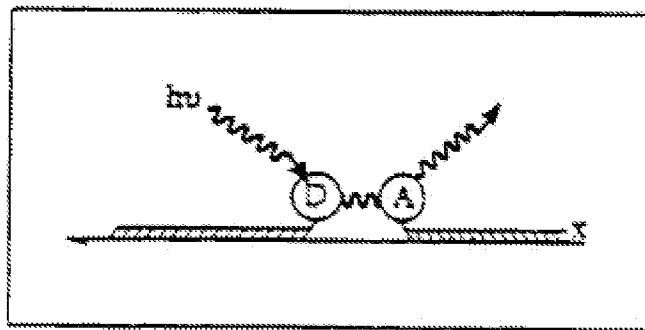


Fig. 3B

In Wittwer's approach, one has to look at the signal emitted from the acceptor in order to get a meaningful result. If one instead looked at the signal emitted by the donor, as suggested by the Examiner, one would obtain a signal whether or not the target sequence of interest was present in the sample. As such, even in view of Tyagi, one of

ordinary skill in the art would not be motivated to look at the signal of the donor as taught in the pending claims as opposed to the acceptor in a two probe system as taught Wittwer.

Furthermore, Tyagi discloses a "molecular beacon" probe which, like Wittwer's two probe FRET system, provides a positive signal only when the target sequence of interest is present. Tyagi's probes are illustrated in FIG. 1 of Tyagi, which is reproduced below:

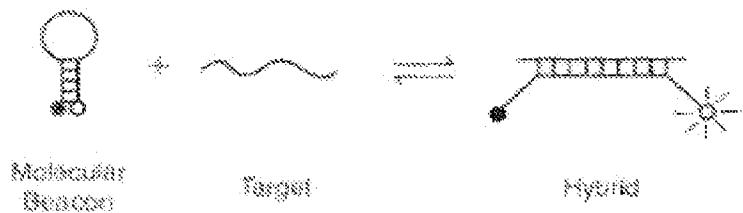


Figure 1. Operation of molecular beacons. On their own, these molecules are nonfluorescent, because the stem hybrid keeps the fluorophore close to the quencher. When the probe sequence in the target hybridizes to its target, forming a rigid double helix, a conformational reorganization occurs that separates the quencher from the fluorophore, recovering fluorescence.

Tyagi's molecular beacons would therefore be viewed by one of skill in the art as a complete substitute for the two probe FRET system as disclosed in Wittwer.

Because Tyagi's molecular beacons would be viewed by one of ordinary skill in the art as a substitute for Wittwer's FRET system, if one of ordinary skill in the art were to modify Wittwer in view of Tyagi, one would in fact replace the two probes of Wittwer with a signal molecular beacon probe of Tyagi.

However, this modification would not teach or suggest the element of the quencher probe as claimed that is distinct from the signal probe whose signal is directly detected. There is no reason in Tyagi modified Wittwer system to include a separate quencher probe as such a quencher would have no purpose.

As such, the only reasonable modification that would be made to the Wittwer system by one of ordinary skill in the art following Tyagi's teaching would be to substitute the molecular beacon probes of Tyagi for the two probe FRET system of Wittwer. However, such a system would still not anticipate the claims as amended.

As Didenko was cited solely for the teaching that DABCYL fluorescence quenching is not FRET-related, Didenko fails to make up for the deficiency in the combined teaching of Wittwer and Tyagi.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko fails to teach or suggest all elements of the claimed invention. Therefore, Claims 1-4, 6, 9-12, 14-15, 26-28, 31-33, 36-44 and 46-56 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and this rejection may be withdrawn.

The Examiner has rejected Claims 5 and 7-8 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and Caplin. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of melting temperature differences between probes. For this element, the Examiner looks to Caplin.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Caplin was cited solely for the element of melting temperature differences between probes, Caplin fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Caplin fails to teach or suggest all elements of the claimed invention. Therefore, Claims 5 and 7-8 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Caplin and this rejection may be withdrawn.

The Examiner has rejected Claim 13 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Sokol. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of hairpin probes. For this element, the Examiner looks to Sokol.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Sokol was cited solely for the element of hairpin probes, Sokol fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Sokol fails to teach or suggest all elements of the claimed invention. Therefore, Claim 13 is not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further view of Kubista and this rejection may be withdrawn.

The Examiner has rejected Claims 16-20 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Kubista. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of linear self-indicating signal probes. For this element, the Examiner looks to Kubista.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Kubista was cited solely for the element of linear self-indicating signal probes, Kubista fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Kubista fails to teach or suggest all elements of the claimed invention. Therefore, Claims 16-20 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further view of Kubista and this rejection may be withdrawn.

The Examiner has rejected Claims 21-23 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Tyagi et al., U.S. 6,277,607 (henceforth “Tyagi B”). The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of an intercalating dye. For this element, the Examiner looks to Tyagi B.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Tyagi B was cited solely for the element of an intercalating dye, Tyagi fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Tyagi B fails to teach or suggest all elements of the claimed invention. Thus, Claims 21-23 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Tyagi B and this rejection may be withdrawn.

The Examiner has rejected Claims 24-25 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Singer. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element a fluorescent minor groove binding dye. For this element, the Examiner looks to Singer.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Singer was cited solely for the element of a fluorescent minor groove binding dye, Singer fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Singer fails to teach or suggest all elements of the claimed invention. Therefore, Claims 24-25 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further view of Singer and this rejection may be withdrawn.

The Examiner has rejected Claims 29 and 34 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko further in view of Elenitoba-Johnson. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of the temperature rate change. For this element, the Examiner looks to Elenitoba-Johnson.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Elenitoba-Johnson was cited solely for the element of the temperature rate change, Elenitoba-Johnson fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Elenitoba-Johnson fails to teach or suggest all elements of the claimed invention. Therefore, Claims 29 and 34 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Elenitoba-Johnson and this rejection may be withdrawn.

The Examiner has rejected Claims 30 and 35 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Wittwer B. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of the rate of monitoring the detectable signal. For this element, the Examiner looks to Wittwer B.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Wittwer B was cited solely for the element of the rate of monitoring of the detectable signal, Wittwer B fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Wittwer B fails to teach or suggest all elements of the claimed invention. Therefore, Claims 30 and 35 are not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Wittwer B and this rejection may be withdrawn.

The Examiner has rejected Claim 45 under 35 U.S.C. §103(a) as allegedly being unpatentable over Wittwer in view of Tyagi as evidenced by Didenko and further in view of Schalasta. The applicants respectfully traverse this rejection.

In making this rejection, the Examiner asserts that the primary combination of references teaches all of the elements of the claims but for the element of virus genotyping. For this element, the Examiner looks to Schalasta.

However, as demonstrated above, the primary references fail to teach or suggest the claimed invention, in that direct detection of the signal from the signal probe and/or the presence of a quencher probe distinct from the signal probe is neither taught nor suggested by the cited combination of teachings. As Schalasta was cited solely for the element of virus genotyping, Schalasta fails to make up for this deficiency.

Accordingly, the combined teaching of Wittwer in view of Tyagi as evidenced by Didenko and further in view of Schalasta fails to teach or suggest all elements of the claimed invention. Therefore, Claim 45 is not obvious under 35 U.S.C. §103(a) over Wittwer in view of Tyagi as evidence by Didenko and further in view of Schalasta and this rejection may be withdrawn.

### **CONCLUSION**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 01-2213, order number BP0208-US.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 16, 2008

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